UPDATED INTERIM GUIDELINES FOR:

PREVENTION OF THE SPREAD OF PANDEMIC (H1N1) 2009 INFLUENZA INFECTION IN THE HEALTHCARE SETTING

CLINICIAN IDENTIFICATION & MANAGEMENT OF PATIENTS

CDC, WHO, and Other Guideline Adaptation for Long Beach-area Facilities

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I. Background

On June 11, 2009, the World Health Organization (WHO) declared that a pandemic (Global Pandemic Phase 6) is occurring due to human cases of a novel strain of influenza. Initially called Swine Origin Influenza virus (S-OIV), this infection is now conventionally designated as Pandemic (H1N1) 2009 Influenza. Infections due to the virus have been confirmed in residents of all U.S. states and throughout the world. Furthermore, widespread influenza activity has continued through the summer in California, a period not usually associated with influenza activity in the Northern hemisphere.

Signs and symptoms in most patients continue to be consistent with those of influenza-like illness (ILI) - fever and respiratory tract illness (cough, sore throat, & runny nose), headache, muscle aches - and some cases have had vomiting and diarrhea. Although the majority of cases have been mild, similar to seasonal influenza, severe respiratory disease, including fatal outcomes, continues to be manifest.

II. Introduction

These guidelines contain modifications and adaptations of guidelines promulgated by the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO). They also incorporate the recently released Aerosol Transmissible Diseases (ATD) Standard from Cal/OSHA. These modifications attempt to address, in a practical yet evidence-based manner, the realities and constraints which are likely to be encountered in healthcare facilities. Increases in clinical and laboratory demands, combined with existing and potential shortages of healthcare personnel and materiel are expected to limit a facility's ability to implement nationally issued guidelines. As circumstances do allow, facilities are encouraged by Long Beach Department of ealth and Human Services (LBDHHS) to follow such guidelines. It should be noted, that the Cal/OSHA standard and associated regulation (General Industry Safety Orders § 5199) represents a true mandate and supersedes any earlier requirements commenting on related topics. This specifies the utilization of N95 masks in the healthcare setting.

III. Case Definitions for Infection with Pandemic (H1N1) 2009 Influenza A Virus - as Adapted by LBDHHS

A ***confirmed case*** is defined as a person with an acute febrile respiratory illness with lab-confirmed Pandemic (H1N1) 2009 infection at CDC or California Department of Public Health (CDPH) Viral/Rickettsial Disease Laboratory (VRDL)* by one or more of the following tests:

1. Real-time RT-PCR
2. Viral culture

Currently, it is recommended that only ***hospitalized*** cases with ILI, or ***deaths*** associated with ILI have specimens submitted for testing for Pandemic (H1N1) 2009. Specimens submitted from deceased patients should preferably be placed in non-formalin based media.

A ***probable case*** had previously been defined as a person with an acute febrile respiratory illness who is positive for influenza A, but negative for H1 and H3 by influenza RT-PCR (non-typeable). Currently, these cases are considered to be equivalent to those confirmed.

A clinically ***suspected case*** of Pandemic (H1N1) 2009 infection is defined: as a person with acute febrile respiratory illness with onset within 7 days of close contact (within 3-6 feet) with a person who is a confirmed/probable case of Pandemic (H1N1) 2009 infection.

A ***suspected case*** for infection control purposes in a health care setting (for deciding which patients warrant presumptive isolation),

> Any patient less than 60 years of age with a fever (>37.8C or 100F) and new onset of cough
>
> *OR*
>
> Any patient whom a health care provider believes, based on the patient's history and illness, to have a high likelihood of being infected with pandemic (H1N1) 2009 influenza virus.

Influenza-like Illness (ILI) = Acute febrile respiratory illness: recent onset of at least two of the following: temperature ≥ 100°F (T ≥ 37.8°C), cough, rhinorrhea or nasal congestion, sore throat.

IV. Pandemic (H1N1) 2009 Exclusion Period

- Persons should be considered potentially contagious until 24 hours after resolution of fever (without concurrent use of antipyretics). This represents the amount of time which a person with ILI should stay away from work, school, or other public settings (camps, mass gatherings, etc.).
- This exclusion period does not apply to the healthcare setting. In healthcare settings, isolation practices should be maintained for 7 days, or resolution of fever, whichever is longer. This recommendation is not affected by administration of antiviral agents.
- Persons who continue to be ill longer than 7 days after illness onset should be considered potentially contagious until symptoms have resolved.

- Younger children and immunocompromised persons might potentially be contagious for longer periods.
- The duration of infectiousness (period of viral shedding) may vary by influenza strain.

V. Pandemic (H1N1) 2009 Transmission

- Transmission of Pandemic (H1N1) 2009 virus is being studied as part of the ongoing outbreak investigation. The data available continue to indicate that this virus is transmitted in ways similar to other influenza viruses.
- Seasonal human influenza viruses seem to be spread from person to person primarily through large-particle (> 5 μm in size) respiratory droplet transmission (e.g., when an infected person coughs or sneezes near a susceptible person).
- Transmission via large-particle droplets requires close contact between a source and recipient, because droplets do not remain suspended in the air and generally travel only a short distance (<1 meter / 3 feet) through the air.
- The transmission of influenza viruses through small-particle aerosols (droplet nuclei) at distances > 3 feet cannot be definitively excluded based on available experimental and observational studies. Because of this consideration, respirators, such as particulate respirators at 95% efficiency may provide additional protection in certain situations where procedures such as endotracheal intubation, suctioning, bronchoscopy or nebulizer treatments of infected patients may lead to creation of aerosolized particles in the vicinity of the patient.
- Contact with respiratory-droplet contaminated surfaces is another likely source of transmission. Because data from Pandemic (H1N1) 2009 are limited, the potential for ocular, conjunctival, or gastrointestinal infection is unknown.
- All respiratory secretions and bodily fluids (diarrheal stool) of Pandemic (H1N1) 2009 influenza cases should be considered potentially infectious.

VI. Infection Control of Ill Persons outside of a Healthcare Setting

Non-hospitalized ill persons who are a confirmed or suspected case of Pandemic (H1N1) 2009 influenza infection are recommended to stay at home (voluntary isolation) until 24 hours after the resolution of fever (without use of fever-reducing medications), except to seek medical attention.

VII. Infection Control of Ill Persons in a Healthcare Setting

1. Meticulous handwashing with soap and water (for ≥ 20 seconds), or use of alcohol-based waterless hand sanitizing agent should be viewed as the primary means of influenza prevention both within and outside the confines of the healthcare setting.

2. Patients with ILI (acute, febrile respiratory illnesses) should be segregated from other patients and staff until evaluated by a physician.

3. Such patients can be placed in a private room with the door closed, if such a room is available, or and a mask should be provided, if available.

4. Healthcare workers (especially those who perform such duties as evaluation, diagnosis, treatment, transport, housing, or management) who "directly contact and interface" with patients infected with aerosol transmissible pathogens (e.g., a *novel* influenza virus) must comply with standards as described in the California Department of Industrial Relations website in the Occupational Safety and Health Standards Board section at: http://www.dir.ca.gov/oshsb/atd).html. It is possible that this Cal/OSHA standard may not be applicable if the CDC declares that the Pandemic (H1N1) 2009 influenza virus is no longer *novel*.

5. If available, an airborne infection isolation room (AIIR) with negative pressure air handling with 6 to 12 air-exchanges per hour can be used. Air can be exhausted directly outside or be recirculated after filtration by a high efficiency particulate air (HEPA) filter. If such rooms are unavailable, a private patient room with a closed door is considered an acceptable alternative.

6. The ill person should wear a surgical mask when outside of the patient room, and should be encouraged to wash hands frequently and follow respiratory hygiene/cough etiquette practices.

7. Patients who are suspected/probable/confirmed cases of Pandemic (H1N1) 2009 influenza should be maintained in isolation until:
   a. Pandemic (H1N1) 2009 influenza is excluded by laboratory testing (PCR, not rapid tests)
   b. A plausible alternative diagnosis is established as the explanation for the illness in the patient
   c. The patient's symptoms have resolved, or 7 days have elapsed from symptom onset, whichever is longer.
   d. The patient is discharged to home isolation

8. Guidelines for reuse of N95 Respirators are expected to be forthcoming. In the interim period, N95 respirators may be considered for reuse if they a) are not visibly soiled, b) are not grossly misshapen (i.e. crumpled in a pocket), c) are not wet or damp, d) are retained for use by the same worker (i.e. not shared), are donned and doffed without touching the inner surface.

   Under scenarios where shortages of N95 Respirators and/or other PPE exist, hospitals may request additional resources. This may be done through the Long Beach Disaster Resource Centers (DRCs) under the auspices of the Healthcare Preparedness Program (HPP). The Long Beach DRCs are St. Mary's Medical Center (contact: Kathy Crow), and Long Beach Memorial Medical Center (contact: J.C. Arzaga). Facilities not covered under HPP may contact the LBDHHS to request further resources.

9. Patients with respiratory failure being supported with closed-circuit mechanical ventilation may still generate droplets/aerosols if circuit is inadvertently disrupted, or intentionally disconnected during respiratory treatments (e.g. suctioning).

10. Disposable gloves should be worn during care of patients with suspected/probable/ confirmed Pandemic (H1N1) 2009 influenza. Glove use, however, does not eliminate the

need for handwashing or hand sanitizer use after all patient contact. Gloves must be removed after each contact with a patient or secretions.

11. If there is an extreme scarcity in private isolation rooms, patient cohorting can be considered for implementation. Patients with comparable underlying conditions (similar immunological baseline states, comorbidities) with ILIs, or suspected Pandemic (H1N1) 2009 influenza infections can be placed in the same hospital room/treatment area, but beds should be separated by at least 3 feet.

12. Cups and other utensils used by the ill person should be washed with soap and water before use by other persons. Routine cleaning and disinfection strategies used during influenza seasons can be applied to the environmental management of Pandemic (H1N1) 2009 influenza.

VIII. LBDHHS ADAPTATIONS OF CLINICIAN GUIDANCE

Objective:
This is provided for clinicians caring for patients suspected or confirmed to have infection due to Pandemic (H1N1) 2009 influenza.

Clinical Findings:

Among those infected with Pandemic (H1N1) 2009 influenza, clinical syndromes have ranged from mild respiratory illness, to lower respiratory tract illness, dehydration, or pneumonia. The majority of patients have had uncomplicated disease with fever, headache, upper respiratory tract symptoms (cough, sore throat, and rhinorrhea), myalgias, and fatigue. Significant gastrointestinal symptoms (diarrhea, vomiting) have been reported, predominantly in younger children. Although the proportion of patients with H1N1 infection requiring hospitalization is not exactly known, approximately 80% of those hospitalized have had underlying medical conditions.

Complications:

Clinicians can expect complications to be similar to seasonal influenza:

- Exacerbation of underlying chronic medical conditions
- Upper respiratory tract disease (sinusitis, otitis media, croup)
- Lower respiratory tract disease (pneumonia, bronchiolitis, status asthmaticus); secondary bacterial pneumonia with or without sepsis
- Cardiac (myocarditis, pericarditis)
- Musculoskeletal (myositis, rhabdomyolysis)
- Neurologic (acute and post-infectious encephalopathy, encephalitis, febrile seizures, status epilepticus, Reye Syndrome)
- Toxic shock syndrome

Pneumonia due to Pandemic (H1N1) 2009 influenza:

The majority of patients admitted to hospitals have shown radiographic evidence of pneumonia. Preliminary analysis of case series has identified some trends among this subset of patients with severe disease.

Groups at high risk for complications:

A signature feature of pandemic influenza is that younger people are disproportionately affected by infections with a novel strain of influenza virus, with older people likely harboring residual immunity from influenza strains infecting them during *their* childhoods. Thus, the highest rates of infections have been seen in those less than 24 years of age, and high rates of hospitalizations seen in very young children.

Largely, many of the risk groups who are at higher risk for seasonal influenza complications should also be considered at higher risk for Pandemic (H1N1) 2009 influenza complications. While pregnancy, chronic heart or lung disease and immunosuppresion are considered risk factors for severe disease associated with influenza, the numbers of persons with severe disease who have morbid obesity (BMI ≥ 35) is a finding rather unique to this pandemic. Conditions with demonstrated higher risk for pandemic influenza morbidity/mortality:

- Persons with chronic lung disease (i.e. asthma, COPD)
- Hemodynamically significant cardiac disease (hypertension alone is not a risk)
- Pregnancy
- Obesity (BMI ≥ 35)
- Metabolic diseases (e.g. diabetes mellitus)
- Immunosuppressive disorders/receipt of immunosuppressive agents
- Neuromuscular disorders

It is presumed that these conditions also are at increased risk for influenza complications:

- Diseases that requiring long-term aspirin therapy
- Chronic renal dysfunction
- Cancer
- Neurological or cognitive disorders which may compromise the handling of respiratory secretions.

Testing of patients for Pandemic (H1N1) 2009 Influenza virus

In an effort to focus lab resources, the WHO, CDC, and the CDPH have issued revised guidelines for submitting specimens.

1. At this time, testing at LBDHHS Public Health Laboratory (PHL) will be focused on:
   - Hospitalized patients
   - Deceased persons with Pandemic (H1N1) 2009 suspected to be a cause of death (or a contributor to cause of death)
   - Patient is part of a cluster of people with ILI (only ONE patient needs laboratory confirmation)

2. Clinicians should test suspected cases of Pandemic (H1N1) 2009 fitting the above criteria by obtaining one of the following specimens (LBDHHS PHL has validated a new viral transport medium for transporting routine specimens for Pandemic H1N1 testing):

   - A nasopharyngeal swab or wash/aspirate (preferred specimen)
   - A nasal wash/aspirate
   - A tracheal aspirate
   - An aspirate obtained via bronchoscopy (BAL)

3. A specimen should optimally be collected within the first 24-72 hours of onset of symptoms. In a hospitalized patient in whom Pandemic (H1N1) 2009 influenza is considered in the differential diagnosis, however, a specimen should be submitted as soon as possible and oseltamivir initiated presumptively (without waiting for laboratory results) Such a scenario may be a patient with community-acquired pneumonia who is deteriorating/not improving on standard anti-bacterial therapy.

4. If a patient meets the criteria for laboratory testing under these guidelines, please submit specimens to the LBDHHS PHL; specimens should be submitted with a completed specimen collection form and third party payer information, if applicable.

5. Patients without symptoms consistent with ILI should NOT be tested (i.e., in order to "clear" a person for work or school attendance).

6. Patients should NOT be sent to LBDHHS for testing.

7. Several commercial laboratories also offer the RT-PCR for Pandemic (H1N1) 2009 (e.g. Quest).

8. Specimens from deceased patients may be submitted fresh frozen (submitted in dry ice) or fixed in formalin (submitted at room temperature). A minimum total of 8 blocks or fixed tissue specimens from the following sites should be submitted for evaluation (please notify LBDHHS PHL in advance if transporting specimens from deceased patients):

    - Central (hilar) lung with segmental bronchi
    - Right and left primary bronchi
    - Trachea (proximal and distal)
    - Representative pulmonary parenchyma from left and right lung

9. For questions on specimen collection, transport, and testing, please calls the LBDHHS Public Health Lab at (562) 570-4080.

Rapid Influenza Diagnostic Tests (RIDT) for Pandemic (H1N1) 2009

Several rapid, point-of-care commercial assays for detection of influenza are widely available in hospitals and other healthcare facilities. Different test kits have different capabilities. Some can distinguish between infections due to influenza A and those due to influenza B; others can only detect infections due to influenza A; finally, there are kits which can only determine the presence or absence of influenza, unable to distinguish A from B. It is important to note that none of these kits can distinguish subtypes of influenza A (i.e. distinguish H3N2 from H1N1). Moreover, these RIDT's have variable ability to detect infection due to Pandemic (H1N1) 2009 influenza (sensitivity ranges 40 – 69%) when compared to RT-PCR.

At the current time, when Pandemic (H1N1) 2009 influenza constitutes the overwhelming proportion of circulating influenza strains, a positive RIDT for influenza A can be cautiously viewed as presumptive evidence of infection due to the pandemic strain. Such patients with either severe infection or at significantly increased risk of complications, can reasonably receive antiviral therapy. Hospitalized patients, however, should have formal testing with Influenza RT-PCR to confirm infection.

A negative result from a RIDT, however, does **not** rule out infection with Pandemic (H1N1) 2009 influenza. If there is strong clinical suspicion that the patient is infected with Pandemic (H1N1) 2009 influenza, in the context of an appropriate diagnostic evaluation, confirmatory RT-PCR should be sent, and antiviral therapy considered.

Treatment for Pandemic (H1N1) 2009 Influenza

This influenza virus strain appears to be susceptible to both oseltamivir (Tamiflu) and zanamivir (Relenza). It is resistant to amantadine and rimantadine. Isolated cases of resistance to oseltamivir have been reported, most recently among severely immunocompromised patients in Seattle, so clinicians caring for immunosuppressed patients with H1N1 patients should be aware of the potential for development of antiviral resistance and prolonged viral shedding.

1. The overwhelming majority of patients with Pandemic (H1N1) 2009 have recovered without any anti-viral therapy.
2. Not all patients with ILI require empiric antiviral therapy.
3. Patients with cold symptoms, but no fever, should NOT be prescribed antiviral drugs.
    a. These drugs may be in SHORT SUPPLY, so overuse of these drugs may make them unavailable for other people who are seriously ill.
    b. These drugs may have significant side effects (neuropsychiatric and/or gastrointestinal symptoms prominent among them).
    c. Flu viruses frequently develop resistance to these drugs, rendering them useless.
    d. Anti-viral drugs are not “cure-alls”; they may shorten the length of illness by ~ 1-2 days.
    e. These agents are most effective in preventing deaths and severe complications so they are most useful in hospitalized/seriously ill persons, and those at heightened risk for complications.
4. The standard dose of oseltamivir for adults is 75 mg Q 12 hours x 5 days. The drug has been found to be most effective when begun within 48 hours of symptom onset. Thus, if used, they should be started at the earliest presumption of infection due to influenza, without waiting for confirmatory tests. In critically ill patients who present > 48 hours after onset of symptoms, antiviral drugs should nonetheless be initiated, as their benefits will outweigh risks in that setting.
5. Preliminary data suggest that for those patients with severe manifestations of infection, or morbid obesity (BMI ≥ 35), higher doses of oseltamivir (150 mg Q12 hours), or courses longer than 5 days may be advisable.
6. In older children and adults who are considered candidates for anti-viral therapy, zanamivir (Relenza), may be prescribed.
    a. The patient should be able to cooperate with the inhalational route of administration.
    b. Relenza can exacerbate bronchospasm in asthmatic patients. Thus, this drug should be avoided in this population.

7. Although oseltamivir is listed by the FDA as a pregnancy category "C" agent, it is very likely that the benefits of its administration in pregnant women in any trimester outweigh any risks to the fetus. Thus, pregnant women presenting with ILI should be considered candidates for presumptive therapy with oseltamivir. This therapy should be initiated as soon as the diagnosis is suspected, without waiting for results of confirmatory testing.

Additional Therapy
Additional therapy such as antibacterial agents should be used at the discretion of the clinicians given the patients clinical presentation.

Results of sputum gram stain analysis may inform decision-making. If a good quality specimen (abundant neutrophils, scant epithelial cells) demonstrates an abundant, dominant bacterial morphology, this may support a presence of bacterial pneumonia in a patient presenting with an ILI and evidence of pneumonia.

Fatalities which occurred during the 1918-1919 influenza pandemic have been recently reanalyzed. It has been demonstrated that a significant proportion of these deaths were due to bacterial co-infection/superinfection. Involved pathogens prominently included *Streptococcus pneumoniae*, *Haemophilus influenzae*, beta-hemolytic Streptococci, and *Staphylococcus aureus.* Such information may assist clinicians who may be considering use of adjunct anti-bacterial agents. It should be noted that early data of hospitalized patients with H1N1 have not found very high rates of bacterial co-infection or superinfection. Interpretation of this is clouded by the fact that the majority of patients admitted to the hospital have received anti-bacterial agents irrespective of admission sputum gram stain/culture results and other laboratory data.

Antiviral Chemoprophylaxis
Factors mitigate against the widespread use of chemoprophylaxis for influenza:

a. The potential for shortages of antiviral medications,
b. The risk of adverse effects associated with oseltamivir, especially in children
c. The risk of development of antiviral resistance in evolving influenza strains

Thus, chemoprophylaxis should be utilized ***very judiciously***. Chemoprophylaxis should be undertaken only for exposed individuals who are at high risk for severe disease, complications, and death due to influenza. The adult dose for oseltamivir for chemoprophylaxis is 75 mg Daily x 10 days.

IX. Vaccination for Pandemic (H1N1) 2009 Influenza:

Once effective vaccine for Pandemic (H1N1) 2009 influenza is available, it will be offered to certain target groups in Long Beach which comprise about 50% of the city population. Strategic and operational plans will be available as federal and state plans crystallize.

X. For More Information:

For more information about Pandemic H1N1 and surveillance activities, please contact: John Holguin at (562) 570-4302 or Erin Salce at (562) 570-4344.For more information regarding clinical and isolation guidelines, please contact Dr. Anne Anglim at (562) 570-4290.

References are available upon request.

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